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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/468,002	12/20/1999	PAUL NEGULESCU	AURO1130-2	3109

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EXAMINER
LANDSMAN, ROBERT

ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/468,002	Applicant(s) NEGULESCU ET AL.	
	Examiner Robert Landsman	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *63-123* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *63-123* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Formal Matters

A. Amendment B, filed 8/29/01, has been entered into the record.

B. Claims 63-109 were pending in this application. New claims 110-123 have been added. Therefore, claims 69-123 are pending.

C. All 35 USC Statutes not found in this Office Action can be found, cited in full, in a previous Office Action.

Withdrawn Claim Rejections

1. Claim Rejections - 35 USC § 112, first paragraph – written description

A. The rejection of claims 63-109 under 35 USC 112, first paragraph, has been withdrawn since the artisan could conceive of the amino acid sequence of any protein which is at least 70% identical to SEQ ID NO:2.

2. Claim Rejections - 35 USC § 112, second paragraph

A. The rejection of claims 63-109 under 35 USC 112, second paragraph, regarding the term "Gα15" has been withdrawn since Applicants have identified this protein by SEQ ID NO.

B. The rejection of claims 71-79, 89 and 90 under 35 USC 112, second paragraph, regarding the term "substantially" has been withdrawn since Applicants have removed this term from the claims.

3. Claim Rejections - 35 USC § 103

A. All rejections under 35 USC 103 have been withdrawn in favor of the rejections under 35 USC 112, first paragraph.

Maintained Claim Rejections

1. Claim Rejections - 35 USC § 112, first paragraph – scope of enablement

A. Claims 63-109 remain rejected and new claims 110-123 are also rejected under 35 USC 112, first paragraph, for the reasons already of record on pages 2-3 of the Office Action dated 3/27/01. Applicants argue that working examples are not necessary to enable the breadth of the claims under 35 USC 112, first paragraph and that the claimed methods can be practiced without undue experimentation. Applicants did amend the claims to recite that the Gα15 protein is at least 70% or 80% identical to SEQ ID NO:2. While this does limit the scope of the claims and does provide some guidance as to the structure of the G protein, it is unpredictable to one of ordinary skill in the art how to make a functional Gα15 protein which can have as many as 113 amino acids of the 374 amino acid-long protein of SEQ ID NO:2 either altered, added, substituted, or deleted. Applicants provide no guidance or working examples of functional Gα15 proteins other than SEQ ID NO:2.

Therefore, due to the lack of guidance and working examples of what amino acid residues are critical to maintain the function (e.g. G protein coupling) of a Gα15 other than SEQ ID NO:2, it is unpredictable to the artisan of how to make a functional Gα15 of SEQ ID NO:2 which is altered by as much as 30% and which retains the biological functions of SEQ ID NO:2. It is suggested that the recitation of "at least 70%" and "at least 80%" should be amended to "at least 95%" or higher, and should also be amended to also recite that the Gα15 retains it G protein-coupled receptor-binding ability.

2. Claim Rejections - 35 USC § 112, second paragraph

A. Claims 63-109 remain rejected and new claims 110-123 are also rejected under 35 USC 112, second paragraph, for the reasons already of record on pages 4-5 of the Office Action dated 3/27/01. Applicants have amended claims 63, 71, 75, 81, 90 and 94 to clarify the detection step. However, as seen in claim 63(iii), for example, the detection of a change in reporter gene function before and after addition of "said ligand" does not necessarily indicate that this ligand is acting through the GPCR of interest. In addition, an additional step should be added to these claims which demonstrates that the change in reporter gene expression, for example, that its increase (or decrease) signifies that the ligand is a ligand for the GPCR in question.

B. Claims 79 and 89 remain rejected under 35 USC 112, second paragraph, for the reasons already of record on page 5 of the Office Action dated 3/27/01. Applicants argue that the phrase "target protein" is explicitly defined on page 23, lines 2-12. However, the definition provided is for target "polypeptides" and not "proteins." Second, the target polypeptide is defined as a GPCR on page 23. Since the claims of this application are directed towards GPCRs, it is suggested that replacement of the phrase "target protein" with "GPCR," "target GPCR,"or "target GPCR polypeptide" would be remedial.

New Claim Rejections

2. Claim Rejections - 35 USC § 112, first paragraph - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claims 63, 71, 75, 81, 90, 94 and 102 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one

skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

First, these claims do not recite that the GPCR has to be transfected into the cell. While Applicants do provide examples in the specification of how to detect GPCRs and their activity, Applicants have not taught the artisan how to identify a ligand to a specific endogenously expressed GPCR among all the various types of endogenously expressed GPCRs in that cell. There is no guidance or working examples of how the artisan would be able to identify which specific receptor was binding and being activated by, the test ligand, nor would it be predictable to the artisan how to determine the exact receptor being bound and activated by the ligand. The specification does mention, for example Example 6 of the specification, that the effect of the ligand on GPCRs can be inhibited by antagonists. However, this does not identify the specific GPCR affected by the test ligand, only that a particular family, or, at most, subfamily, of GPCRs is being activated.

Furthermore, the way the claims are written, it appears that the Gα15 protein is able to directy cause the activation of a reporter gene. Applicants have not explained how the Gα15 protein of the invention is able to enter the nucleus to activate a gene, nor have they provided a link as to how this protein would be able to induce (or inhibit) reporter gene expression.

Therefore, in summary, due to the lack of guidance of how Gα15 affects reporter gene expression, along with the lack of guidance and working examples, as well as the unpredictability of how one of ordinary skill in the art would be able to identify a specific receptor which has been activated by a given test ligand, the Examiner holds that undue experimentation would be necessary to practice the invention as claimed.

2. Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 63-123 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 63, 64, 66-72, 74-76, 78-82, 84-91, 93-95, 97-103 and 105-123 are confusing since it appears that, even though the claims appear to imply that the GPCR, reporter gene and Gα15 are not endogenously expressed in the cell, the claims are not limited to transfected cells and read on cells which endogenously express any or all of these components. This is further supported by the fact that claims 65, 73, 77, 83, 92, 96 and 104 specifically recite that the GPCR is not naturally expressed in the cell, implying that it may be endogenous in the independent claim. With respect to embodiments in which the GPCR is endogenously expressed in the cell, the claims are incomplete because they do not teach sufficient steps to determine which GPCR is affected by the test ligand or chemical since cells comprise more than one type of GPCR. Similarly, Applicants have not addressed the issue of how to determine which GPCR was a target for a test ligand given that cells normally express numerous types of endogenous GPCRs.

B. Claims 67-70, 74, 78, 80, 84-88, 93, 97-101 and 105-109 are also indefinite since it is not clear at what time point in the method steps these additional steps are performed. In addition, it is not clear what a "reporter gene substrate" is, or how contacting the cell with said substrate, or with the compounds of claims 68-70, 78, 80, 84-88, 93, 97-101 and 105-109 will provide the necessary information regarding the relationship between the GPCR, ligand and/or test compound or chemical.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
November 19, 2001

Gary L. Kunz
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